

**REMARKS**

Claims 12 and 28 have been amended to make more definite. Claim 25 has been amended to address the examiner's objection and provide proper antecedent basis. Claim 26 has been amended to correct a typographical error. It is believed that none of these amendments constitute new matter and their entry is requested.

Applicant appreciates the Examiner's efforts to advance prosecution by examining new claims 26-28.

**SPECIFICATION**

Applicant has amended paragraph [0002] in order to correct an administrative error in the proper identification of government interest.

**CLAIM OBJECTIONS**

Claim 25 has been amended as required by the Examiner to further clarify that the DNA fragment is fused to the BCG hsp60 gene, and to provide proper antecedent basis for the promoter. Withdrawal of this objection is therefore requested.

**35 USC § 112, second paragraph**

Claims 12 and 28 have been rejected in the Office Action under 35 USC § 112, second paragraph, as being indefinite for failing to particularly print out and distinctly claim the subject matter of the invention.

Claim 12 has been rejected as indefinite for recitation of "genetic mycobacterium variants thereof". Applicant has amended claim 12 in order to clarify that it is naturally occurring or genetically modified mycobacterium of the listed strains, and any subspecies thereof, that are intended to be claimed.

Claim 28 has been rejected as indefinite for recitation of "producing a microorganism with an altered level of D-alanine ligase expression relative to a non-transformed microorganism." Claim 28 has been amended to clarify that it is the level of D-alanine ligase expression of a corresponding non-transformed microorganism that is intended to be claimed. Withdrawal of the rejections under 35 USC § 112, second paragraph are therefore requested.

**35 USC § 112, first paragraph**

Claims 24 and 25 have been rejected under 35 USC § 112, first paragraph, for lack of enablement. Applicant traverses this rejection and asserts that the recombinant mycobacterium and the vector of claims 24 and 25 require the use of biological materials that are capable of being prepared by one skilled in the art without undue experimentation from readily available starting materials using the description in the instant specification.

More specifically, the *E.coli* shuttle vector pMV262 was publicly known through publications, such as Connell et al., 90 *Proc. Natl. Acad. Sci.* 11473-11477 at 11477 (December 1993) (copy attached as Exhibit 1), which identifies the publicly available source of the pMV262 vector. In fact, the instant invention was constructed using pMV262 from the same source, MedImmune, Inc. (See Table 1 and paragraph [00105]). Both vector and sequences were available from MedImmune, Inc. MedImmune, Inc. has now transferred rights in pMV262 back to Albert Einstein College of Medicine from where the public now has ready access. Furthermore, Connell et al. describe the main components of pMV262: origins of replication, kanamycin gene and hsp60 promoter. The sequences of each of these components are also known. The kanamycin resistance gene is in the public database at NCBI (accession P00551) and is published (aph gene from Th903) in Oka et al., *J. Mol. Biol.* 1981 Apr 5 147(2):217-26 at 222. The sequence of hsp60 is published in Shinnick, *J. Bacteriol.* 1987 Mar 169(3):1080-1288.

The sequence of the pAL5000 origin of replication is in the public database at NCBI (accession NC-001381) and is published in Rauzier et al. *Gene*. 1988 Nov 30 71(2):315-321; and the *E-coli* origin of replication, pUC19, is published in Yanisch-Perron et al. *Gene.*, 1985 33(1):103-119. Copies of each of these references are attached hereto as Exhibits 2-7, respectively.

Furthermore, the sequence of pMV262 is contained within pBUN276 (on deposit with ATCC as PTA-8190). pBUN276 is inserted into the polylinker site of pMV262. pMV262 has the same polylinker site described for pMV261. The sequence for pMV262 is published in Stover, et al., *Nature*, 1991 Jun 6, 351.456-460 at Figure 1a (attached Exhibit 8).

In summary, the *E.coli* shuttle vector pMV262 is described in the literature and the nucleic acid sequences of the vector components are known and readily available. 37 C.F.R. 1.802(b) provides that deposit is not necessary if a material is "known and readily available to the public or can be made or isolated without undue experimentation." If the starting material is generally available, and the biological material can be made and used by one skilled in the art with reference to the application, deposit is not required. *Amgen Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 1211 (1991).

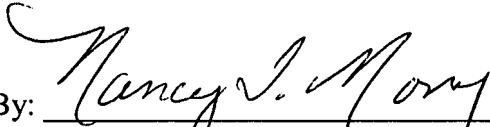
One skilled in the art could make and use mycobacterium strain GPM265 following repeatable methods set forth in the application (see Examples 1 and 2 and Table 1), using available starting materials - strain MC<sup>2</sup> 155 is publicly available from ATCC (designated MC(2)155) (Exhibit 9) - and the pBUN276 plasmid is on deposit with ATCC and designated PTA-8190. As such, no deposit is required (27 C.F.R. 1.802(b)). When an organism is created by insertion of genetic material into a cell obtained from generally available sources, all that is required is a description of the means of carrying out the invention. *Amgen*, 927 F.2d (a) 1211. That some experimentation is necessary does not constitute lack of enablement as long as it is

not unduly extensive. *Atlas Powder Co. v. E. I. duPont De Nemours & Co.*, 750 F.2d 1569, 1576 (Fed. Cir. 1984).

Applicants further point out that the information on both the plasmid and GPM265 is described in the manuscript filed with the related provisional application (Feng and Barletta, 2003 Jan; *Antimicrobiol Agents and Chemotherapy*, 47(1):283-291). In order to publish in this journal, applicants were required to agree to distribute both the plasmid pMV262 and GPM265 to the public. As requested by the examiner, Applicant clarifies that ATCC deposit designated PTR-8190 does not contain GPM265.

In view of the foregoing amendments and remarks, it is respectfully submitted that the claims now presented are patentable over the prior art of record and therefore in condition for allowance and eventual issuance. Such action is respectfully requested. Should the Examiner have any further questions or comments which need be addressed in order to obtain allowance, please contact the undersigned attorney at the direct number listed below.

Respectfully submitted,

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